

# The Langer-Giedion Phenotype Associated with a Unique Skeletal Finding in a Mentally Retarded Adolescent Male

## A Case Report

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### SUMMARY

A case of a mentally retarded male patient with associated physical abnormalities resembling the multiple exostoses-mental retardation syndrome (MEMR, Langer-Giedion or Ale-Calo syndrome) is reported. The patient represents one of the most severe examples of this condition; he also has a triphalangeal thumb with double distal phalanges, a feature not reported previously.

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A full diagnostic work-up of mentally retarded patients with physical stigmata is of value because of genetic counselling, prognostication, and possible guidance in family planning for the parents. The association of mental retardation with multiple epiphyseal dysplasia, exostoses, retarded growth and microcephaly suggested the diagnosis of the Langer-Giedion syndrome in one of our male patients.<sup>1</sup> Genealogical studies did not indicate parental consanguinity, affected family members, or increased paternal age. The appearance of an autosomal dominant condition in a patient whose parents, siblings and grandparents are normal usually suggests a new mutation; thus no further recurrence of the same condition is expected in this family. Because the well-known phenotypic variation in dominant conditions may complicate clinical diagnosis, it was thought worth while to report this patient who suffers from the most severe manifestations of the syndrome.

### CASE REPORT

The patient, an 18-year-old White male with severe mental retardation, is in an institution.

He was born normally at term, cried immediately after birth, and was never cyanosed or jaundiced. The mother apparently had a severe attack of influenza when she was 4 months pregnant. Little is known about the developmental history. He was admitted to hospital at the age of 2 years when it was noted that he appeared to be mentally retarded. He could not walk and had loose

joints. He could only say 'mamma' and 'pappa'. The mother had noticed a lump in his abdomen since he was 1 year old, but his scrotum remained empty.

On admission, examination revealed a microcephalic, mentally retarded child. His head circumference and weight were both below the 3rd centile. There was a double thumb on the left hand and he had a peculiar facies with a broad nose and very small nostrils. Palpation of the abdomen revealed a mass just below the umbilicus, and cryptorchidism. The joints appeared to have an increased range of movement. There were no abnormal bony growths at that stage.

At laparotomy, a large cyst arising from the posterior aspect of the prostate and adherent to the inferior part of the bladder was seen. Both testes were present. Histological examination showed that the cyst had developed from Müllerian duct remnants. One of the testes was so closely associated with the tumour that it had to be removed as well. The testis was histologically infantile in type but in one section there was intratubular proliferation of Sertoli-like cells which suggested an androblastoma. No evidence of malignancy was found.

At the age of 13 years he was admitted to an institution where mentally retarded children are cared for, and where he has been ever since. It is not known when visible exostoses first appeared. When we first saw him at the age of 17 years he appeared healthy. He had a peculiar facies with a broad nasal bridge and lop ears. (Fig. 1). He was of short stature, and microcephaly and multiple tumorous swellings on the limbs were present (Fig. 2). Deficient shoulder girdle musculature was noted. His weight (31 kg), height (134 cm) and head circumference (47 cm) indicated microcephaly and growth retardation. Sexual maturity appeared normal.

According to the AGS Vineland Social Maturity Scale his social quotient was 7,3, corresponding to an age equivalent of 15 months. A radiographic skeletal survey revealed multiple exostoses (Fig. 3) involving the hip and knee joints, upper shaft of the humerus, distal shafts of the radius and ulna, and some of the tubular bones of the hand. The hip joint displayed epiphyseal dysplasia on both sides. A triphalangeal thumb was seen on the left hand. Cone-shaped epiphyses were present in the phalanges of the hands and feet. The distal phalanges of the hands showed sclerotic epiphyses (Fig. 4). The bone age of the hands and feet was retarded. A congenital block vertebra in the C2-C3 region was seen, and hemivertebrae were present in the mid-dorsal and distal dorsal segments, with deficiency of their neural arches. Oblique hypoplastic ribs were observed on the straight chest radiograph (Fig. 5).

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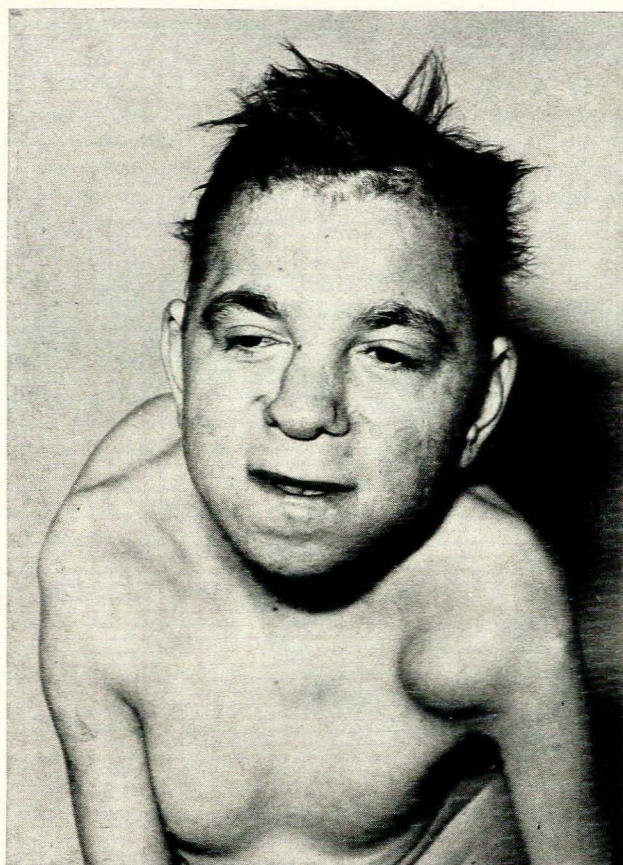


Fig. 1. Facial appearance showing broad nasal bridge, lop ears and microcephaly.

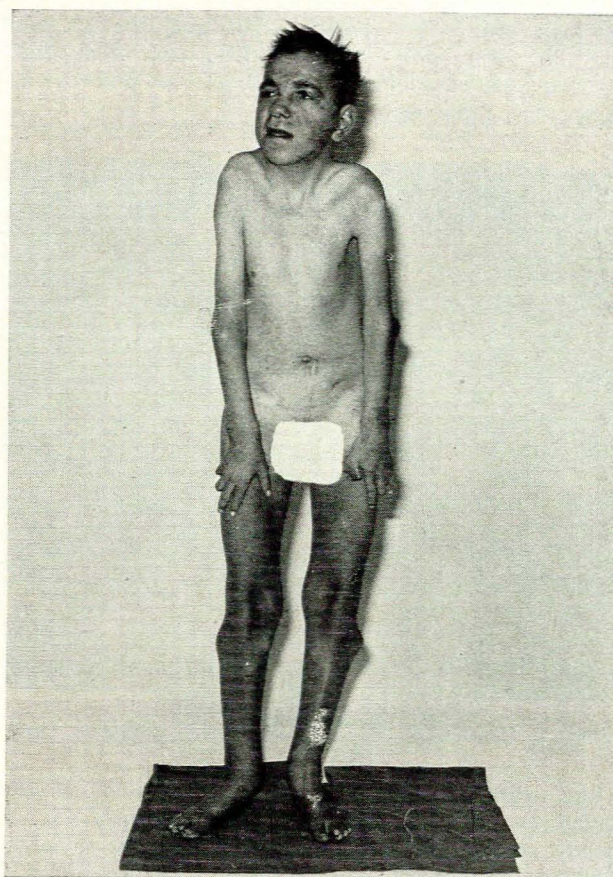


Fig. 2. Exostoses are visible as bony tumours on the limbs.

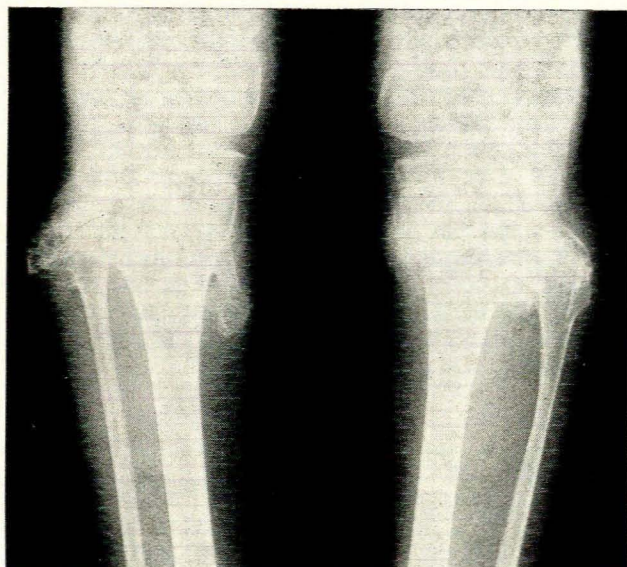


Fig. 3. Radiograph showing multiple skeletal exostoses.

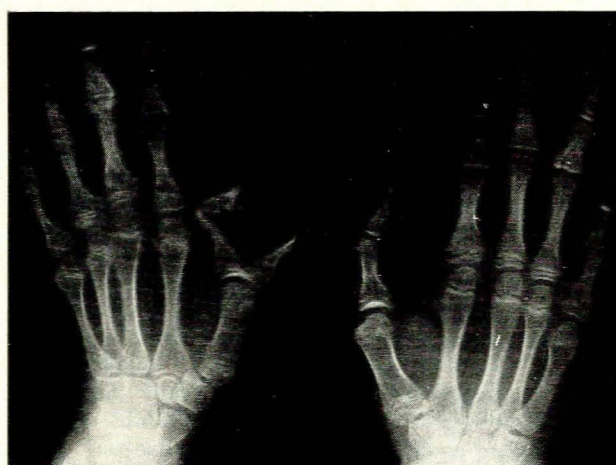


Fig. 4. Radiograph showing phalangeal cone-shaped epiphyses with sclerosis and retarded bone age.

## DISCUSSION

The differential diagnosis of this condition may be reviewed under the following headings: (i) the epiphyseal



dysplasia group; (ii) conditions affecting the epiphyses and soft tissue; (iii) other conditions associated with a triphalangeal thumb; (iv) the acrodysplasias; and (v) other causes of multiple exostoses.

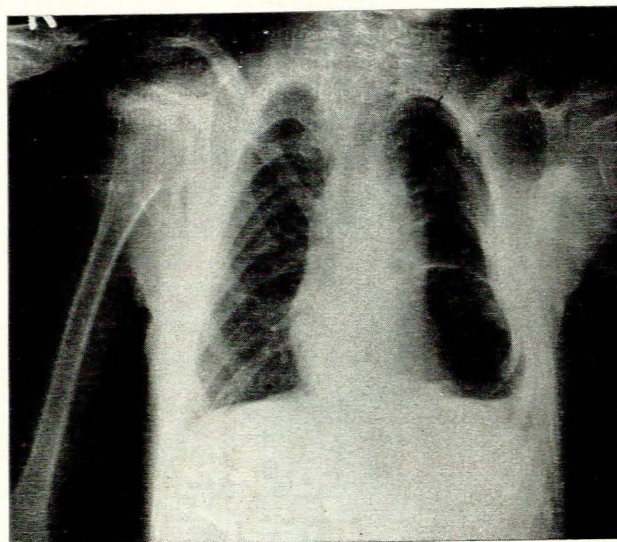


Fig. 5. Radiograph showing oblique hypoplastic ribs.

**The epiphyseal dysplasia group.** The epiphyseal dysplasias are divided into two major groups:<sup>2</sup> (a) the spondylo-epiphyseal dysplasias which affect the spine and epiphyses and result in shortening of stature owing to loss of truncal height; and (b) the multiple epiphyseal dysplasias which affect mainly the epiphyses, resulting in some loss of height but rarely in severe stunting. None of the various syndromes included in this group is associated with the findings demonstrated in our patient. These epiphyseal dysplasias also have to be differentiated from other genetic conditions affecting the epiphyses, such as Morquio's syndrome, achondroplasia and pseudo-achondroplasia in which spinal and pelvic morphological variations may aid in the differential diagnosis. Associated clinical findings make identification of cretinoid epiphyseal dysgenesis, dysplasia epiphysialis hemimelia and diastrophic dwarfism obvious.

**Conditions affecting the soft tissues and epiphyses.** In patients with these conditions one has to exclude juvenile rheumatoid arthritis radiologically. The latter condition usually involves the knees, ankles and wrists rather than the hips, which are always involved in epiphyseal dysplasias. Another dramatic condition simulating milder epiphyseal dysplasia is arthrogryposis multiplex congenita.

**Conditions associated with a triphalangeal thumb.** Morphological variations of triphalangy are associated with additional abnormalities, such as an atrial septal defect in the Holt-Oram syndrome. A triphalangeal thumb with double phalanges has been reported in a grandfather, son and grandson.<sup>3</sup> Such a thumb was also seen in our patient and represents a new association not listed in McKusick's<sup>4</sup> directory of genetic diseases, although triphalangeal thumbs have been linked with aplastic anaemia

in this publication.<sup>4</sup> Our patient had a normal haematological profile.

**The acrodysplasias.** This group of conditions is characterized by some type of dysplastic development, mainly of the most peripheral part of the extremities.<sup>5</sup> The presence of phalangeal cone-shaped epiphyses of the hands or a peculiar, juvenile, phalangeal epiphyseal necrosis is required for the diagnosis. Because of these cone-shaped epiphyses, our patient had the requirements for inclusion into this group as regards two possible conditions, the trichorhinophalangeal syndrome or the Langer-Giedion syndrome (*vide infra*).

**Other causes of multiple exostoses.** Multiple cartilaginous exostoses associated with normal intelligence, short metacarpals and Madelung's deformity of the forearm is a well-known entity, also known as diaphyseal aclasis.

**Results of clinical analysis.** The only situation in which multiple exostoses are found in association with other abnormalities is the multiple exostoses-mental retardation syndrome (MEMR, Langer-Giedion or Ale-Calo syndrome). The most important signs of this condition are mental retardation, microcephaly, shortened stature with asymmetry, peculiar facies, muscular hypoplasia with hyperextensibility at the peripheral joints, multiple exostoses, epiphyseal dysplasia and cone-shaped epiphyses. This condition is best suited to the findings in our patient (P. M. Beighton — personal communication). According to Kozlowski *et al.*<sup>1</sup> this must also be differentiated from the trichorhinophalangeal syndrome which consists of ear anomalies, brachyphalangy with deformities of the fingers, wedge-shaped epiphyses and mental dullness.<sup>6</sup> This, however, is not associated with exostoses.

## CONCLUSION

As in other situations in clinical medicine, proper evaluation of the lesions and a specific diagnosis aid in the management and prognosis of retarded patients as well as in family counselling. This should take place as soon as possible, when family planning may still be affected by the genetic information. It is disheartening to learn from a study by Thurmon *et al.*<sup>7</sup> on the diagnostic evaluation of 2 000 institutionalized persons with mental retardation, that only a small number of families notified of counselling facilities took advantage of the latter. Non-motivated parents may form part of the home background which was responsible for institutionalization in the first instance. Therefore, emphasis is laid on provision of genetic counselling services as soon as possible after the patient's birth or after his admission to an institution.

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